



INTENSIVE COMPUTATIONS HELP US UNDERSTAND THE BRAIN



At Tampere University of Technology, Finland, a great deal of innovative computational research is carried out. One of the internationally ambitious research areas is computational neuroscience and neuroinformatics. In Tampere, researchers look at complex interactions within neuronal molecular networks as well as within the networks of neurons and glial cells. One example of such studies is how intracellular IP3 receptor-ion channel protein complexes affect the intracellular calcium dynamics and, subsequently, the information processing and learning in small dendritic spines of neurons. A future research area of such studies involves examining how delicate processes are disrupted in neuronal dysfunctions that occur, for example, in Alzheimer's disease and Down's syndrome.

- We have systematically built a basic understanding on earlier work in the field. We aim to take this knowledge to the next level and eventually provide information that will contribute to how to tackle specific pathological diseases, says Marja-Leena Linne, leader of the Computational Neuroscience Laboratory (CNSL) within the Computational Systems Biology Research Group at the Department of Signal Processing.

From 'in vitro' to 'in silico'

The research has been limited by two factors. The primary one is the limited amount of data on specific neuronal processes, especially related to human subjects. The second is the limited scope of models used and the restrictions on the computational power available for simulating more advanced models. One example are the models that take stochasticity into account.

- As the brain is the most complex living system we know of, it is of great importance to collect both in vivo and in vitro data at different levels of abstraction. This work is undergoing internationally. A great challenge is to organize it in ways that allow both structural and functional aspects to be combined. We are, for example, doing in vitro work with standard cultured human and non-human cells and combine microscopes and electrophysiological equipment to understand maturation, growth, and modification of neuronal networks in vitro, says Marja-Leena Linne.

- We need to record with many channels and obtain images at different phases of development. The challenge with our studies is the speed of analyzing and processing the acquired data into a form of information suitable for building complex models of neuronal functions.

In data-driven research fields, such as the neurosciences, experimental research is always necessary. The far more efficient research method to test different hypothesis and complex interactions is, however, computational simulation, the 'in silico'. It helps researchers to develop models with which it is easier to understand the function of neural systems at different levels of abstraction. However, as the research requires a great number of variables in order to, for example, stochastically simulate large neuronal networks, their growth and activity accurately, not enough computing power has been available.

Creating and simulating multi-scale models is a computationally heavy task and for that reason research areas have been limited. But the research environment is changing in Tampere with more and more computing power to tackle the big questions: how does the brain work and what are the



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mechanisms for learning and formation of memory at the global and local network levels in comparison to single neuron level.

An essential tool and a competitive advantage

Distributed computing technology is now a tool without which the various research groups at Tampere University of Technology would not be able to carry out their research either at all or at a much slower pace.

- We combine computation-based neuroscience with theoretical and experimental neurosciences. We start with existing biological models that take into account the stochasticity inherently present in biological systems. Here we find Techila's fast distributed computing a necessity.

- With this distributed computing technology we expect to gain in many areas of modeling and data analysis. When developing computational models we can do reliable parameter estimation within a reasonable time frame. We can analyze the role of stochasticity in neuronal processes. On the other hand, we are able to run sophisticated data analysis tasks, says Marja-Leena Linne.

- To give one example, Tiina Manninen who works as Postdoctoral Researcher of the Academy of Finland has been able to cut the computing time of a neuronal signaling model to a revolutionary extent with Techila. Previously, using a single PC for a specific simulation would have taken seven years to complete, and now we get results in six days, says Marja-Leena Linne. – The results were also reliable and accurate compared to previous approximations.

- We do extremely ambitious research purely on the basis of computation. In our future research, we are going to look at how big a role a single neuron has in a network of neurons. We already know that simple neuronal networks can modify their behavior depending on the incoming stimulus and, ultimately, to show properties similar to learning new patterns of information presented to the network. Currently we are setting up the computing environment for such computational heavy simulations.

- At Tampere University of Technology, specifically the groups involved in doing computational research and large-scale simulations, feel privileged with their computational capacity. Their staff has not previously had access to similar distributed computing systems that are very user-friendly and easy to manage. This will further enhance the university's attractiveness internationally as a research center.

- The amount of computational testing of biological hypotheses will quite obviously increase when powerful computing resources become available. New application areas will also be expanded on when distributed computing technology's potential is understood to the full and models can be adjusted to best reflect the reality, says Marja-Leena Linne.

- There is no doubt about what a competitive edge we have with Techila Distributed Computing Solution in the fiercely time-critical world of research and publications.

Personal Profile: Dr. Marja-Leena Linne

- Adjunct Professor, Department of Signal Processing, Tampere University of Technology
- Coordinator of INCF National Node of Finland, 2010-11
- Academy research fellow, Acad. of Finland, 2004-09

Selected Publications

- A. Saarinen*, M.-L. Linne*, O. Yli-Harja., Stochastic Differential Equation Model for Cerebellar Granule Cell Excitability. PLoS Computational Biology 4(2): e1000004 (2008) *Equal contribution
- T. Manninen, M.-L. Linne, K. Ruohonen, Developing Itô stochastic differential equation models for neuronal signal transduction pathways. Computational Biology and Chemistry 30(4):280-291 (2006)
- A. Pettinen, O. Yli-Harja, M.-L. Linne. Comparison of automated parameter estimation methods for neuronal signaling networks. Neurocomputing 69(10-12) 1371-1374 (2006)

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